Remarks

Claims 1-2, 4-5, 8-10, 12, 14-16, 18-20, 24, and 26-27 have previously been cancelled. Claims 3, 6, 11, 13, 17, 22-23, 25 and 28-32 remain under examination in the application. Claims 13, 25, and 28 have been amended.

Claims 13 and 28 have been amended to specify a particular group of subjects to which the method applies and to indicate that a sufficient amount of the formulation is administered to those subjects to mediate inflammation. Claim 13 recites adult subjects and claim 28 recites infant subjects. In this way, the subject population has been limited in a manner that was recommended by the Examiner during the telephonic interview held on August 19, 2009. The subject population is now limited to individuals having an inflammatory bowel disorder, having a disorder arising from an allergic response, having a disease involving an epithelial surface response, or having inflammation of the intestine, retina, or neuronal tissue. Support for this amendment can be found in paragraph 243, for example. Example 3 provides data showing what amounts of the ganglioside diet is sufficient. Applicants submit that it has not previously been recognized that subjects having one of the above noted disorders or conditions would derive benefit from the specified formulation of gangliosides at the indicated dosage. Nor have any studies shown what amounts, if any, of the recited formulations would be sufficient to mediate inflammation when administered orally to such subjects. As pointed out in the specification previous studies do not explain whether dietary gangliosides can be absorbed and used for EPL synthesis (¶ 291) which leads to an anti-inflammatory effect (¶ 293).

Claim 25 has been amended to be restricted to a particular group of adults: those with elevated cholesterol. In this way, the subject population has been limited in a manner that was recommended by the Examiner during the telephonic interview. The adult subject population is now limited to individuals having a need for plasma cholesterol lowering because of elevated cholesterol levels. Applicants submit that it has not previously been recognized that subjects having elevated cholesterol would derive benefit from the specified formulation of gangliosides at the indicated dosage. Thus, it follows that no studies have indicated what amounts, if any, of the recited formulations would be sufficient to lower cholesterol when administered orally to such subjects

Information Disclosure Statement

The Examiner has noted that references listed on pages 7 to 13 of the application have not been considered. The Applicant has provided, under separate cover, an Information Disclosure Statement submitting these references. References cited in an International Search Report have also been submitted.

35 U.S.C. 103

The rejection of the claims as being unpatentable over the combination of (1) Ettinger in view of (2) Pan et al. and (3) the Merck Manual of Diagnosis and Therapy is believed to be traversed with the amendments put forward herein.

Each of the independent claims (claims 13, 25 and 28) has been amended to define a subject population to which the method is directed and to require administration of a sufficient amount of the recited formulation to reduce cholesterol (claim 25) or mediate inflammation (claims 13 and 28). Ettinger lacks any teaching of amounts of its dietary supplements that could have the recited therapeutic effects. Ettinger does not teach that GD3 is present at the level of at least 50% in a formulation of gangliosides, nor is there a restriction placed on the subject population to be subjects having inflammatory bowel disorders, disorders arising from allergic responses, diseases involving epithelial surface responses, or inflammation of the intestine, retina, or neuronal tissue. Ettinger has neither provided a formulation in which GD3 is the predominant ganglioside, nor provided a ganglioside formulation to address any of the four stated categories of conditions to which the subject population is restricted. Lastly,

While Ettinger teaches a reduction in the number of gastrointestinal disease producing organisms using a ganglioside formulation, there is no implication that mediating inflammation or reducing plasma cholesterol per se would be possible. Applicants respectfully submit that reducing inflammation, reducing plasma cholesterol of the present claims are distinct from Ettinger's teaching of reducing the number of gastrointestinal disease producing organisms. These are distinct biological effects which are achieved through distinct mechanisms.

With regard to the formulation itself, there is no implication that a fraction containing GD3 is considered for use in Ettinger. GM1, GD1a and GT1 fractions are all considered, but there is no implication that GD3 may be a possible candidate for use in a formulation, much less the predominant ganglioside in the formulation, as now recited in each independent claim of the

instant application. Specific gangliosides and amounts are not described by Ettinger. The study of Pan et al. that simply describes ganglioside composition from various sources does not provide any indication to use any particular ganglioside formulation or any target therapeutic use for any particular ganglioside formulation as is now required in the amended claims. Thus, the combination of Ettinger and Pan *et al.* would not permit a skilled person to arrive at the subject matter of the claims. By merely combining teachings of Merck regarding *E. coli* infection as a cause for inflammation with Pan *et al.* and Ettinger, there is no further incentive for a person skilled in the art to arrive at the claimed invention. Although reducing bacterial *E. coli* infection may be a cause of inflammation, Applicants submit that a person having skill in the art still would not have an expectation that the recited formulations would directly reduce inflammation or plasma cholesterol much less understand what amounts would be necessary to do so.

For these reasons Applicants respectfully request the Examiner to reconsider the basis for the rejection and withdraw the rejection as to claims 13 and 28 and their dependent claims 3, 6, 7, 11 and 29-32.

Claims 17, 21-23 and 25 stand rejected as unpatentable over Berger et al., as made of record in the previous action. The arguments put forward in the previous response are again reiterated herein with the additional distinction that the population of subjects to which the inventive method applies has now been limited in a way that is not taught or disclosed by Berger et al. Specifically, Berger et al does not suggest that a population of adults having elevated plasma cholesterol would derive any benefit from consumption of ganglioside formulations of the composition now specified, nor does Berger disclose any amount of its composition that would be effective for doing so.

Berger *et al.*, appears to describe a ganglioside containing composition that is colostrum-derived and which appears to have binding activity toward pathogens. This is not the subject of claim 25, or the claims depending therefrom, and thus because claim 25 relates to cholesterol lowering Applicants respectfully submit that Claim 25 is distinct from Berger *et al.* Further, there is no suggestion by Berger *et al.* that its gangliosides which are provided in the colostrum of the hyperimmune milk product should be predominantly GD3 as recited in claim 25. The mention of GD3 is made only in the context of it being one of two gangliosides (GM3 and GD3) found in the product, but not in the context of it being the predominant ganglioside.

Applicants submit that claim 25 and its dependent claims 17 and 21-23 which contain all of its limitations are distinct and patentable over Berger for these reasons and requests withdrawal of this rejection.

Double Patenting

Claims 17, 21-23 and 25 stand rejected for nonstatutory obviousness-type double patenting over claims 1-5 of U.S. Patent No. 6,998,392. Applicants submit that pending claim 25 is limited to the treatment of patients needing to reduce their plasma cholesterol levels as opposed to claims 1-5 of the '392 patent which are limited to the treatment or prevention of *Giardia* infection. Applicants respectfully submit that there is no overlap in the patient populations. Moreover, Applicants respectfully submit that reducing plasma cholesterol and reducing the number of gastrointestinal disease producing organisms are distinct biological effects achieved through distinct mechanisms. Applicants submit that one of skill in the art simply would not have any reasonable expectation that a method useful for treating *Giardia* would also be useful for reducing cholesterol.

A petition for a three month extension of time is included in today's submission. Applicants respectfully submit that the application is in condition for allowance and earnestly request the same. Should the Examiner identify any issues that could be resolved by a telephone call the Examiner is urged to call the undersigned to expedite prosecution.

Respectfully submitted,

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